

IN THE CLAIMS:

Please cancel claims 182 to 184 without prejudice or disclaimer and add new claims 433-486 as shown below.

1-181. (Previously cancelled)

182-184. (Currently cancelled)

185-432. (Previously cancelled)

433. (New) A composition comprising at least two types of nanoparticles having oligonucleotides attached thereto, at least a portion of the oligonucleotides on a first type of nanoparticles having a sequence complementary to a sequence of a first portion of a target nucleic acid, and at least a portion of the oligonucleotides on a second type of nanoparticles having a sequence complementary to a sequence of a second portion of the nucleic acid.

A2
434. (New) The composition of Claim 433 wherein the target nucleic acid is viral RNA or DNA.

435. (New) The composition of Claim 433 wherein the target nucleic acid is a gene associated with a disease.

436. (New) The composition of Claim 433 wherein the target nucleic acid is a bacterial DNA.

437. (New) The composition of Claim 433 wherein the target nucleic acid is a fungal DNA.

438. (New) The composition of Claim 433 wherein the target nucleic acid is a synthetic DNA, a synthetic RNA, a structurally-modified natural or synthetic RNA, or a structurally-modified natural or synthetic DNA.

439. (New) The composition of Claim 433 wherein the target nucleic acid is from a biological source.

440. (New) The composition of Claim 433 wherein the target nucleic acid is a product of a polymerase chain reaction amplification.

441. (New) The composition of Claim 433 wherein the target nucleic acid comprises one or more types of linking oligonucleotides.

442. (New) The composition of Claim 441 wherein the linking oligonucleotide is single-stranded.

443. (New) The composition of Claim 441 wherein the linking oligonucleotide is double-stranded and has overhanging ends.

AA
cont.
444. (New) The composition of Claim 441 wherein the linking oligonucleotide is a triple-stranded oligonucleotide connector.

445. (New) The composition of Claim 441 wherein the linking oligonucleotide comprises a peptide nucleic acid chain.

446. (New) The composition of Claim 433 wherein the oligonucleotides are attached to the nanoparticles in a stepwise ageing process comprising (i) contacting the oligonucleotides with the nanoparticles in a first aqueous solution for a period of time sufficient to allow some of the oligonucleotides to bind to the nanoparticles; (ii) adding at least one salt to the first aqueous solution to create a second aqueous solution; and (iii) contacting the oligonucleotides and nanoparticles in the second aqueous solution for an additional period of time to enable additional oligonucleotides to bind to the nanoparticles.

447. (New) The composition of Claim 447 wherein the second aqueous solution has an ionic strength sufficient to overcome at least partially the electrostatic attraction or repulsion of the oligonucleotides for the nanoparticles and the electrostatic repulsion of the oligonucleotides to each other.

448. (New) The composition of Claim 446 wherein the oligonucleotides and nanoparticles are contacted in aqueous solution for about 12 to about 24 hours.

449. (New) The composition of Claim 446 wherein salt is added to the first aqueous solution to form the second aqueous solution which is buffered at pH 7.0 and which contains about 0.1 M NaCl.

A2
cont. 450. (New) The composition of Claim 446 wherein the oligonucleotides and nanoparticles are contacted in the second aqueous solution for an additional 40 hours to increase the density of oligonucleotides bound to the nanoparticles.

451. (New) The composition of Claim 449 wherein the salt is added to the first aqueous solution in a single addition.

452. (New) The composition of Claim 449 wherein the salt is added gradually to the first aqueous solution over time.

453. (New) The composition of Claim 449 wherein the salt is selected from the group consisting of sodium chloride, magnesium chloride, potassium chloride, ammonium chloride, sodium acetate, ammonium acetate, a combination of two or more of these salts, one of these salts in a phosphate buffer, and a combination of two or more these salts in a phosphate buffer.

454. (New) The composition of Claim 453 wherein the salt is sodium chloride in a phosphate buffer.

455. (New) The composition of Claim 433 wherein the oligonucleotides are present on a surface of the nanoparticles at a surface density of at least 10 picomoles/cm².

456. (New) The composition of Claim 455 wherein the oligonucleotides are present on the surface of the nanoparticles at a surface density of at least 15 picomoles/cm².

457. (New) The composition of Claim 456 wherein the oligonucleotides are present on the surface of the nanoparticles at a surface density from about 15 picomoles/cm² to about 40 picomoles/cm².

A2
CdS.
458. (New) The composition of Claim 433 wherein the nanoparticles are metal nanoparticles or semiconductor nanoparticles.

459. (New) The composition of Claim 458 wherein the nanoparticles are gold nanoparticles.

460. (New) The composition of Claim 458 wherein the semiconductor nanoparticles are made of CdSe/ZnS (core/shell).

461. (New) The composition of Claim 433 wherein at least some of the oligonucleotides on the nanoparticles comprise at least one type of recognition oligonucleotides, each type of recognition oligonucleotides comprising a spacer portion and a recognition portion, the spacer portion being designed so that it is bound to the nanoparticles, the recognition portion having a sequence complementary to at least a portion of a sequence of the target nucleic acid.

462. (New) The composition of Claim 461 wherein the spacer portion has a moiety covalently bound to it, the moiety comprising a functional group through which the spacer portion is bound to the nanoparticles.

463. (New) The composition of Claim 461 wherein the spacer portion comprises at least about 10 nucleotides.

464. (New) The composition of Claim 463 wherein the spacer portion comprises from about 10 to about 30 nucleotides.

465. (New) The composition of Claim 461 wherein the bases of the nucleotides of the spacer portion are all adenines, all thymines, all cytosines, all uracils or all guanines.

466. (New) The composition of Claim 433 wherein at least some the oligonucleotides bound to the nanoparticles comprise at least one type of recognition oligonucleotides, each type of recognition oligonucleotides comprising a sequence complementary to at least one portion of a sequence of the target nucleic acid; and a type of diluent oligonucleotides.

A2
CDU4.
467. (New) The composition of Claim 466 wherein, each type of recognition oligonucleotides comprises a spacer portion and a recognition portion, the spacer portion being designed so that it is bound to the nanoparticles, the recognition portion having a sequence complementary to at least one portion of a sequence of the target nucleic acid.

468. (New) The composition of Claim 467 wherein the spacer portion has a moiety covalently bound to it, the moiety comprising a functional group through which the spacer portion is bound to the nanoparticles.

469. (New) The composition of Claim 467 wherein the spacer portion comprises at least about 10 nucleotides.

470. (New) The composition of Claim 469 wherein the spacer portion comprises from about 10 to about 30 nucleotides.

471. (New) The composition of Claim 467 wherein the bases of the nucleotides of the spacer portion are all adenines, all thymines, all cytosines, all uracils or all guanines.

472. (New) The composition of Claim 467 wherein the diluent oligonucleotides contain about the same number of nucleotides as are contained in the spacer portions of the recognition oligonucleotides.

473. (New) The composition of Claim 472 wherein the sequence of the diluent oligonucleotides is the same as that of the spacer portions of the recognition oligonucleotides.

474. (New) The composition of any one of Claims 433, 461, or 466 wherein the oligonucleotides are bound to the nanoparticles through sulfur linkages.

AA
CDJ+
475. (New) The composition of Claim 433 wherein in the presence of target nucleic acid and under hybridization conditions, the composition forms a complex with the target nucleic acid, the resulting complex having a sharp melting profile and increased melting temperature relative to a comparable complex without nanoparticles to allow for selective discrimination of any nucleotide insertion, deletion or mismatch in the target nucleic acid.

476. (New) A kit comprising composition having at least two types of nanoparticles having oligonucleotides attached thereto, at least a portion of the oligonucleotides on the first type of nanoparticles having a sequence complementary to the sequence of a first portion of a nucleic acid, and at least a portion of the oligonucleotides on the second type of nanoparticles having a sequence complementary to the sequence of a second portion of the nucleic acid.

477. (New) The kit of Claim 433 wherein the target nucleic acid comprises one or more types of linking oligonucleotides.

478. (New) The kit of Claim 477 wherein the linking oligonucleotide is single-stranded.

479. (New) The kit of Claim 477 wherein the linking oligonucleotide is double-stranded and has overhanging ends.

480. (New) The kit of Claim 477 wherein the linking oligonucleotide is a triple-stranded oligonucleotide connector.

481. (New) The kit of Claim 477 wherein the linking oligonucleotide comprises a peptide nucleic acid chain.

A2
ODT.
482. (New) A kit comprising a composition having at least two types of nanoparticles having oligonucleotides attached thereto, at least a portion of the oligonucleotides on the first type of nanoparticles having a sequence complementary to the sequence of a first portion of a linking oligonucleotide, and at least a portion of the oligonucleotides on the second type of nanoparticles having a sequence complementary to the sequence of a second portion of the linking oligonucleotide; and one or more types of linking oligonucleotides.

483. (New) The kit of Claim 477 wherein the linking oligonucleotide is single-stranded.

484. (New) The kit of Claim 477 wherein the linking oligonucleotide is double-stranded and has overhanging ends.

485. (New) The kit of Claim 477 wherein the linking oligonucleotide is a triple-stranded oligonucleotide connector.

486. (New) The kit of Claim 477 wherein the linking oligonucleotide comprises a peptide nucleic acid chain.